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HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
COUNTS, GARY W	
ART UNIT	PAPER NUMBER
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,619	BERGMANN ET AL.	
	Examiner	Art Unit	
	GARY W. COUNTS	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The preliminary amendment filed 08/01/06 is acknowledged and has been entered. Currently, claims 1-9 are pending and under examination.

Advisory Note: It appears that claims 1-12 were submitted 08/01/06 prior to the preliminary amendment of 08/01/06 which listed claims 1-9. There is nothing on the record which sets forth the status of claims 10-12. Therefore, since the status of claims 10-12 are unclear and the preliminary amendment filed 08/01/06 is only directed to claims 1-9, claims 1-9 have been treated for their merits. If applicant intends the cancellation of claims 10-12, then applicant should clearly set forth that claims 10-12 have been cancelled.

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

For example, page 3, line 3 & page 6, paragraph 0018 of the current specification contains embedded hyperlinks.

3. The disclosure is objected to because of the following informalities: The specification on pages 9 and 10, paragraphs 0028 and 0029 uses the phrases "as claimed in claim 1" and "the subject of claims 2 to 12". This practice is not conventional for U.S. Applications. For example, the current application only has 9 claims (claims 1-9). Therefore, the disclosure in the specification does not correlate with the current claims. Claims are subject to amendments and cancellation throughout prosecution which can cause discrepancies between any claims disclosed in the specification and those which may be listed. It is recommended to delete the references to claims from the body of the specification.

Appropriate correction is required.

4. The disclosure is objected to because of the following informalities: The specification on page 10 fails to provide a heading "Brief Description of the Drawings".

Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

5. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

6. Claim 6 is objected to because of the use of an acronyms e.g... TPS, CHP … etc. Although the terms may have art-recognized meaning, the terms do not make clear if applicant intends to claim the prior art definitions. The terms should be defined in their first instance.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because there are no positive active method steps for performing the method and it is unclear what method applicant intends to encompass. If applicant intends method claims, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as obtaining, reacting and detecting. Method claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere cataloging of parts. The claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

Claim 1 provides for the use of a method for the early determination of the risk of mortality of patients in intensive care units for whom the clinical diagnosis is sepsis, severe sepsis or septic shock, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use of "a method for

determination of the risk of mortality of patients", but without any active, positive steps delimiting how this use is actually practiced.

In claim 1 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 1, line 1 the recitation "early determination of risk" is vague and indefinite because the term "early" is a relative term which renders the claim indefinite. The term "early determination of risk" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 4 is vague and indefinite in reciting an open ended range of the cutoff in reciting "310 ng/ml or more."

In claim 5 the recitation "parameter" is vague and indefinite because it is unclear what applicant is trying to encompass. There is no definition provided for the term in the specification and the metes and bounds of the claim cannot be determined. For, example does parameter intend fever, does applicant intend a constant or quantity other than the SOD-1, or a different biomarker? See deficiencies throughout the claims.

Regarding claim 6, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In claim 6 the recitation “the peptide inflammin” there is insufficient antecedent basis for this limitation.

In claim 6 the recitation “the peptide prohormones” there is insufficient antecedent basis for this limitation.

In claim 6 the recitation “the C-reactive protein” there is insufficient antecedent basis for this limitation.

In claim 8, the recitation “the evaluation” there is insufficient antecedent basis for this limitation.

In claim 8, the recitation “the complex” there is insufficient antecedent basis for this limitation.

In claim 9 the recitation “(accelerated test)” is vague and indefinite because it is unclear if the recitation within parenthesis () is part of the claim or not. Further, it is unclear what applicant intends by the term “accelerated test”. The term “accelerated" is a relative term which renders the claim indefinite. The term "accelerated test" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warner et al (Clin. Chemistry 41/6, pgs 867-871, 1995) and Galikowski et al (Research in Surgery, Vol. 6, No. 1, April 1994) in view of Uda et al (EP 0217542).

Warner et al disclose a method for the determination of risk of mortality of patients in intensive care units (e.g. abstract, col 2 (materials and methods)). Warner et al disclose determining enzyme concentrations of superoxide dismutase (SOD) in plasma samples obtained from septic patients. Warner et al discloses that the

superoxide dismutase consists of three isoforms, including SOD1 (Cu/Zn SOD), SOD2 and SOD3). Warner et al disclose comparing the concentrations to a predetermined cut-off and determining increases for prognosis (e.g. abstract, p. 869-871). Warner et al also teaches that catalase (sepsis prognosis parameter) is increased in sepsis and is determined along with SOD

Warner et al differs from the instant invention in failing to teach determining the concentration of SOD-1 (Cu/Zn SOD) in the sample.

Galikowski et al teaches that SOD1 activity is increased during sepsis.

Uda et al teaches that the concentration of SOD1 (Cu/Zn SOD) can be determined in patient samples by means of immunoassays. Uda et al teaches that the immunoassays comprise antibodies specific for SOD1 and can be an ELISA assay utilizing monoclonal antibodies. Uda et al teaches that the ELISA assay utilizes at least one labeled (marked) antibody. Uda et al teaches that the amount of SOD-1 in a patients sample can be detected with good precision and with extremely high specificity and used in diagnostic methods.

Although Warner et al does not specifically teach determining the concentration of SOD1, Warner does teach that SOD1 is included in the increased enzyme activity of SOD during sepsis and Galikowski et al teaches that it is known that SOD1 activity is increased during sepsis. Therefore, as shown by Galikowski et al the increased enzymatic activity of Warner et al would include increase activity of SOD1. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the determination of the concentration of SOD1 as taught by

Galikowski in the method of Warner et al because Uda et al teaches that it is known that SOD1 concentrations can be determined in patient samples with good precision and with extremely high specificity and used in diagnostic methods such as taught in both Warner and Galikowski.

13. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Warner et al., Galikowski et al in view of Uda et al as applied to claims 1-3 and 5 above, and further in view of Valkirs et al (US 2003/0119064).

See above for the teachings of Warner et al., Galikowski et al and Uda et al.

Warner et al., Galikowski et al and Uda et al differ from the instant invention in failing to explicitly teach the cutoff level of 310 ng/ml or more.

Valkirs et al teaches that it is known in the art to use ROC curves and to established cut-off levels and particularly teaches that for any particular marker, a distribution of marker levels for subjects with and without a disease will likely overlap and that under such conditions, a test does not absolutely distinguish normal from disease with 100% accuracy, and the area of overlap indicates where the test cannot distinguish normal from disease. Valkirs et al teaches that a threshold is selected, above which (or below which, depending on how a marker moves with the disease) the test is considered to be abnormal and below which the test is considered to be normal.

It would have been obvious to one of ordinary skill in the art to incorporate ROC curves and determine the optimum threshold level as taught by Valkirs et al with the modified method of Warner et al because the modified method of Warner specifically teaches cut-offs and

Valkirs et al shows that it is known in the art for any particular marker, a distribution of marker levels for subjects with and without a disease will likely overlap and that under such conditions, a test does not absolutely distinguish normal from disease with 100% accuracy, and the area of overlap indicates where the test cannot distinguish normal from disease. With respect to the 310 ng/ml cutoff as recited in the instant claims, the optimum cutoff level can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

14. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Warner et al., Galikowski et al in view of Uda et al as applied to claims 1-3 and 5 above, and further in view of Bohuon (US 5,639,617).

See above for the teachings of Warner et al., Galikowski et al and Uda et al.

Warner et al., Galikowski et al and Uda et al differ from the instant invention in failing to teach that the further parameter is procalcitonin.

Bohuon teaches a method for early detection, detection of the severity and for a treatment-accompanying assessment of the course of a sepsis, as well as means for carrying out such a method using procalcitonin and/or partial peptides thereof in a biological sample of a patient along with the simultaneous determination of calcitonin using immunological procedures using specific antibodies (e.g. abstract, cols 3-5, examples 1-3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the more established parameters of sepsis such as procalcitonin as taught by Bohuon with the modified method of Warner et al because the determination of procalcitonin would provide for further confirmation of sepsis and severity of sepsis.

15. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warner et al., Galikowski et al., Uda et al in view of Bohun as applied to claims 1-3, 5 and 6 above, and further in view of Wagner et al (US 6,329,209).

See above for the teachings of Warner et al., Galikowski et al., Uda et al and Bohun.

Warner et al., Galikowski et al., Uda et al and Bohun differ from the instant invention in failing to teach the simultaneous determination by means of a chip technology and evaluating the results obtained with the aid of a computer program.

Wagner et al disclose arrays and methods for determining analytes in a sample (e.g. abstract, col 2-3, col 9-11, col 32-36). Wagner et al disclose the arrays can be

chips (e.g. col 2, example 1). Wagner et al disclose that arrays are used in immunoassays and detection and evaluation of the results is performed with the aid of a computer (e.g. col 34-35). Wagner et al teaches that this provides for methods to be performed in parallel (col 3). Wagner teaches that this protein array provides the advantage of simultaneously detecting a plurality of proteins in a sample and also provides methods for multianalyte analyses (abstract & col 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate chip arrays and computers as taught by Wagner et al into the modified method of Warner et al because Wagner et al teaches that this provides for methods to be performed in parallel. Wagner teaches that this protein array provides the advantage of simultaneously detecting a plurality of proteins in a sample and also provides methods for multianalyte analyses.

16. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Warner et al., Golikowski et al and Uda et al as applied to claims 1-3, and 5 above, and further in view of Daniels et al (US 2006/0008921).

See above for the teachings of Warner et al., Golikowski et al and Uda et al.

Warner et al., Golikowski et al and Uda et al differ from the instant invention in failing to teach performing the detection with immunochromatographic point-of-care.

Daniels et al teaches immunochromatgraphic test strips and methods for quantifying an analyte of interest in a sample (e.g. abstract, pages 2-4). Daniels et al teaches that immunochromatographic lateral flow or strip tests are well-established

diagnostic tools for detecting analytes (para. 0003). Daniels et al teaches that test strips offer the advantages of a simple, user-friendly format, and rapidly obtained results that are easily interpreted and are well suited for applications such as rapid point-of-care testing (para. 0004).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate immunochromatographic devices such as taught by Daniels et al into the modified method of Warner et al because Daniels et al teaches that immunochromatographic lateral flow or strip tests are well-established diagnostic tools for detecting analytes and that test strips offer the advantages of a simple, user-friendly format, and rapidly obtained results that are easily interpreted and are well suited for applications such as rapid point-of-care testing.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/GAILENE R. GABEL/
Primary Examiner, Art Unit 1641

1/21/2009